

What is claimed is:

1. An isolated peptide comprising the amino acid sequence selected from the general structural formula Ia, Ib, Ic and Id:

Cap-AA8-AA7-AA6-AA5-AA4*-AA3-AA2-AA1*	8-mer	Ia
Cap-AA7-AA6-AA5-AA4*-AA3-AA2-AA1*	7-mer	Ib
Cap-AA6-AA5-AA4*-AA3-AA2-AA1*	6-mer	Ic
Cap-AA5-AA4*-AA3-AA2-AA1*	5-mer	Id

wherein

AA1 is selected from:

- (a) Gly,
- (b) Ala,
- (c) Leu, and
- (d) a small aliphatic amino acid;

AA2 is selected from:

- (a) Phe,
- (b) Tha,
- (c) Cha,
- (d) Tyr,
- (e) Pya,
- (f) Trp, and
- (g) another aromatic amino acid;

AA3 is selected from:

- (a) Leu,
- (b) Cpa, and
- (c) a natural or unnatural aliphatic amino acid;

AA4 is selected from:

- 33 -

- (a) Lys,
- (b) Lys substituted by C<sub>1</sub>-C<sub>17</sub> alkyl, C<sub>5</sub>-C<sub>20</sub> arylalkyl or a C<sub>6</sub>-C<sub>20</sub> aryl radical,
- (c) Orn optionally substituted by C<sub>1</sub>-C<sub>17</sub> alkyl, C<sub>5</sub>-C<sub>20</sub> arylalkyl or a C<sub>6</sub>-C<sub>20</sub> aryl radical, and
- (d) hLys optionally substituted by C<sub>1</sub>-C<sub>17</sub> alkyl, C<sub>5</sub>-C<sub>20</sub> arylalkyl or a C<sub>6</sub>-C<sub>20</sub> aryl radical;

AA5 is selected from:

- (a) Arg,
- (b) Lys,
- (c) Orn,
- (d) hLys,
- (e) His, and
- (f) Lys wherein N<sup>ε</sup> is substituted by one or two radicals selected from C<sub>5</sub>-C<sub>20</sub> alkyl, a linear or branched C<sub>1</sub>-C<sub>6</sub> acyl group, cyclized saturated or unsaturated C<sub>5</sub>-C<sub>20</sub> alkyl, C<sub>5</sub>-C<sub>20</sub> arylalkyl and a C<sub>6</sub>-C<sub>20</sub> aryl radical;

AA6 is selected from:

- (a) Lys,
- (b) hLys,
- (c) Orn,
- (d) Lys wherein N<sup>ε</sup> is substituted by one or two radicals selected from C<sub>5</sub>-C<sub>20</sub> alkyl, a linear or branched C<sub>1</sub>-C<sub>6</sub> acyl group, cyclized saturated or unsaturated C<sub>5</sub>-C<sub>20</sub> alkyl, C<sub>5</sub>-C<sub>20</sub> arylalkyl and a C<sub>6</sub>-C<sub>20</sub> aryl radical, and
- (e) Orn wherein N<sup>δ</sup> is substituted by one or two radicals selected from C<sub>5</sub>-C<sub>20</sub> alkyl, a linear or branched C<sub>1</sub>-C<sub>6</sub> acyl group, cyclized saturated or unsaturated C<sub>5</sub>-C<sub>20</sub> alkyl, C<sub>5</sub>-C<sub>20</sub> arylalkyl and a C<sub>6</sub>-C<sub>20</sub> aryl radical, and
- (f) Pro;

AA7 is selected from:

- (a) Ala,
- (b) Val, and

- 34 -

(c) a natural or unnatural amino acid, or mimetics or isostere thereof;

AA8 is selected from:

(a) Pro,

(b) a natural or unnatural amino acid, or mimetics or isostere thereof; and

the Cap is either not present or selected from:

(a) C<sub>1</sub>-C<sub>8</sub> acyl, and

(b) C<sub>3</sub>-C<sub>8</sub> cycloalkylalkanoyl or furanylacetyl;

and pharmaceutically acceptable salts thereof;

such a peptide being optionally linked to nuclear localization peptide sequences HIV-1 Tat or *Antennapedia* peptide sequence (penetratin);

and the (\*) symbol indicates a site for optional intramolecular linkage via an amide, substituted amide bond or isostere thereof; the resulting compounds being the respective cyclic 5-mers, 6-mers, 7-mers, or 8-mers.

2. An isolated peptide according to claim 1, wherein

AA1 is selected from:

(a) Gly,

(b) Ala, and

(c) Leu;

AA2 is selected from:

(a) Phe,

(b) Tha,

(c) Cha,

(d) Tyr,

(e) Pya, and

(f) Trp;

AA3 is selected from:

- 35 -

- (a) Leu,
- (b) Cpa, and
- (c) a natural aliphatic amino acid;

AA4 is selected from:

- (a) Lys,
- (b) Orn, and
- (c) hLys;

AA5 is selected from:

- (a) Arg,
- (b) Lys,
- (c) Orn,
- (d) hLys, and
- (e) His;

AA6 is selected from:

- (a) Lys,
- (b) hLys,
- (c) Orn;

AA7 is selected from:

- (a) Ala,
- (b) Val, and
- (c) a natural amino acid;

AA8 is selected from:

- (a) Pro,
- (b) a natural amino acid; and

the Cap is either not present or selected from:

- (a) acetyl (Ac), cyclopropylcarbonyl, cyclopropylacetyl (Cpr), pivaloyl, isopropylcarbonyl, isopropylacetyl, 2,2-dimethylbutanoyl (Dmb), levulinoyl, cyclopropylglycinoyl (Cpg), dimethylglycinoyl (Dmg), and
- (b) cyclopentylacetyl, cyclohexylacetyl, cycloheptylacetyl, furanylacetyl;

and pharmaceutically acceptable salts thereof;

- 36 -

such a peptide being optionally linked to nuclear localization peptide sequences HIV-1 Tat or *Antennapedia* peptide sequence (penetratin);  
and the (\*) symbol indicates a site for optional intramolecular linkage via an amide bond;  
the resulting compounds being the respective cyclic 5-mers, 6-mers, 7-mers, or 8-mers.

3. An isolated peptide according to claim 1 comprising:  
the cyclic 5-mer:

Ac-Arg-(Lys-Leu-Phe-Gly), or  
Ac-Lys-(Lys-Leu-Phe-Gly);

the cyclic 6-mer:

Ac-Lys-Arg-(Lys-Leu-Phe-Gly),  
Ac-Lys-Lys-(Lys-Leu-Phe-Gly),  
Cpr-Lys-Arg-(Lys-Leu-Phe-Gly),  
Cpr-Lys-Lys-(Lys-Leu-Phe-Gly),  
Cpr-Lys-(C<sub>5</sub>-C<sub>20</sub>)-Lys-(Lys-Leu-Phe-Gly),  
Cpr-Lys-(C<sub>5</sub>-C<sub>20</sub>)-Arg-(Lys-Leu-Phe-Gly),  
Cpr-Lys-(CH(CH<sub>3</sub>)(C<sub>13</sub>H<sub>27</sub>))-Lys-(Lys-Leu-Phe-Gly),  
Dmb- Lys-(C<sub>5</sub>-C<sub>20</sub>)-Arg-(Lys-Leu-Phe-Gly), or  
Dmb- Lys-(C<sub>5</sub>-C<sub>20</sub>)-Lys-(Lys-Leu-Phe-Gly);

the cyclic 7-mer:

Ac-Ala-Lys-Arg-(Lys-Leu-Phe-Gly),  
Ac-Ala-Lys-Lys-(Lys-Leu-Phe-Gly),  
Cpr-Ala-Lys-Arg-(Lys-Leu-Phe-Gly), or  
Cpr-Ala-Lys-Lys-(Lys-Leu-Phe-Gly);

or

the cyclic 8-mer:

Pro-Ala-Lys-Arg-(Lys-Leu-Phe-Gly),  
Ac-Pro-Ala-Lys-Arg-(Lys-Leu-Phe-Gly),

- 37 -

Ac-Pro-Ala-Lys-Lys-(Lys-Leu-Phe-Gly),  
Cpr-Pro-Ala-Lys-Arg-(Lys-Leu-Phe-Gly), or  
Cpr-Pro-Ala-Lys-Lys-(Lys-Leu-Phe-Gly);

wherein parentheses indicate the residues involved in cyclization;

and pharmaceutically acceptable salts of such peptides.

4. A peptide according to claim 1 or a pharmaceutically acceptable salt thereof for use in a method for the therapeutic treatment of a mammal.
5. An isostere of a peptide according to claim 1 which comprises a cyclic 4-mer ring of sequence (AA4-AA3-AA2-3HP) wherein 3HP is a residue of 3-hydroxypropionic acid and AA2 and 3HP are bonded via a carbon to carbon bond between the alpha carbon of the AA2 and the 3-position of the 3HP, or a pharmaceutically acceptable salt thereof.
6. An isostere of a peptide according to claim 5 which comprises a cyclic 4-mer ring of sequence (AA4-AA3-Phe-3HP) wherein Phe and 3HP are bonded via a carbon to carbon bond between the alpha carbon of the Phe and the 3-position of the 3HP, or a pharmaceutically acceptable salt thereof.
7. An isostere of a peptide according to claim 6 which comprises a cyclic 4-mer ring of sequence (AA4-Leu-Phe-3HP) wherein Phe and 3HP are bonded via a carbon to carbon bond between the alpha carbon of the Phe and the 3-position of the 3HP, or a pharmaceutically acceptable salt thereof.
8. An isostere of a peptide according to claim 7 which comprises a cyclic 4-mer ring of sequence (Lys-Leu-Phe-3HP) wherein Phe and 3HP are bonded via a carbon to carbon bond between the alpha carbon of the Phe and the 3-position of the 3HP, or a pharmaceutically acceptable salt thereof.

- 38 -

9. A pharmaceutical composition comprising a peptide according to claim 1, or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier.

10. A pharmaceutical composition for the treatment of cancer in a mammal comprising, in a therapeutically effective amount, a peptide according to claim 1, or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier.

11. The use of a peptide according to claim 1 or a pharmaceutically acceptable salt thereof for the preparation of a pharmaceutical composition for use in the treatment of cancer.

12. The use of a peptide according to claim 1 or a pharmaceutically acceptable salt thereof in the treatment of cancer.

13. A method for treating cancer comprising administering to a mammal in need of such treatment a therapeutically effective amount of a peptide according to claim 1, or a pharmaceutically acceptable salt thereof.

14. A method of inhibiting the binding of the E2F-1 cell regulatory protein to Cyclin A comprising administering to a mammal in need of such treatment a therapeutically effective amount of a peptide according to claim 1, or a pharmaceutically acceptable salt thereof.